PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference 2021149PC/or | FOR FURTHER ACTION See Form PCT/IPEA/416 | |
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| International application No. PCT/FI2003/000521 | International filing date *(day/month/year)* 26.06.2003 | Priority date *(day/month/year)* 27.06.2002 |
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| Applicant DANISCO SWEETENERS OY et al | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 4 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☒ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☒ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 21.01.2004 | 22.10.2004 |
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Form PCT/IPEA/409 (cover sheet) (January 2004)

INTERNATIONAL PRELIM[redacted]RY REPORT ON PATENTABILITY

International application No.
PCT/[redacted]12003/000521

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-40 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 41-44 received by this Authority on 29-09-2004
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT 2003/000521

**Box No. II Priority**

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The priority is considered valid. Therefore, the documents cited in Box No. VI is of no particular relevance.

INTERNATIONAL PRELIM[redacted]RY REPORT ON PATENTABILITY

International application No.
PCT[redacted]12003/000521

**Box No. V** **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-43 | YES |
| | Claims | - | NO |
| Inventive step (IS) | Claims | - | YES |
| | Claims | 1-43 | NO |
| Industrial applicability (IA) | Claims | 1-43 | YES |
| | Claims | - | NO |

2. Citations and explanations (Rule 70.7)

Relevant documents (from the International Search Report):

D1: Handbook of Industrial Crystallization (Butterworths monographs in chemistry), Chapter 3: The Influence of Impurities and Solvents on Crystallization (D. L. Klug), pages 76 and 83 (ed. Allan S. Myerson; Butterworth-Heinemann, Boston 1993).
D2: US6406546 B1
D3: EP0452238 A2
D4: Mikkonen, H. et al; "Effect of nanofiltration on lactose crystallisation"; Milchwissenschaft 56 (6) 2001, pages 307-310 (BIOSIS AN: PREV200100386913).
D5: US5391299 A
D6: US2002012973 A1

The invention according to present claims 1-43 is directed to a process of removing crystallisation inhibitors from a solution comprising one or more reducing monosaccharide sugars and/or sugar alcohols thereof, characterized in that the solution is subjected to nanofiltration, whereby the reducing sugar and/or corresponding sugar alcohol thereof is recovered in the nanofiltration permeate and the crystallisation inhibitors are recovered in the nanofiltration retentate.

Crystallisation inhibitors are defined in the description as compounds with inhibiting effect on the crystallisation of reducing sugars by adhering to the sugar crystal surface in the crystal growth stage. According to the definition it can mean any compounds, but is preferably compounds with at least one monosaccharide unit more than the reducing sugar, e.g. dimeric and/or oligomeric forms of the reducing sugar.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box No. V

The problem with crystallisation inhibitors in sugar manufacture and purification, and the need for their removal, is well known in the prior art. See for example D1, teaching that raffinose has an inhibiting effect on the crystallisation of saccharose (page 76), and that fructose undergoes irreversible dehydration during the crystallisation process to yield several forms of difructose dianhydride impurities (page 83).

D2 is here considered to represent the closest prior art. D2 describes a process for purification of sugar syrups using nanofiltration. In this process, the disaccharide sucrose, which can be a crystallisation inhibitor, is the wanted compound; but it is separated from invert sugars, including fructose and glucose. Just as in the present application, the monosaccharides end up in the permeate, while the sucrose is found in the retentate. The invention according to claims 1-43 thus differs from the prior art according to D2 in that the disaccharide is the wanted compound while the monosaccharides are not wanted, but otherwise the process of separation is essentially the same. Although the intent of the process in D2 is another than in the present application, it must be considered obvious to the person skilled in the art to use the process in D2 to solve the well known problem of removing crystallisation inhibitors. Therefore, the invention according to claims 1-43 is considered to lack an inventive step in view of D2.

See also D3, describing a process for separating dextrose from impurities such as di- and trisaccharides using nanofiltration. As in the case of D2 and with a similar argument, the invention according to claims 1-43 is considered to lack an inventive step in view of D3 as well.

Documents D4-D6 only describe the general state of the art and are of no particular relevance.

In summary, the invention according to claims 1-43 is novel and industrially applicable, but is considered to lack an inventive step.

**Box No. VI Certain documents cited**

1. Certain published documents (Rule 70.10)

| Application No. Patent No. | Publication date *(day/month/year)* | Filing date *(day/month/year)* | Priority date (valid claim) *(day/month/year)* |
|---|---|---|---|
| WO02053781 A1 | 11.07.2002 | 28.12.2001 | 28.12.2000 |
| WO02053782 A1 | 11.07.2002 | 28.12.2001 | 28.12.2000 |
| WO02053783 A1 | 11.07.2002 | 28.12.2001 | 28.12.2200 |

2. Non-written disclosures (Rule 70.9)

| Kind of non-written disclosure | Date of non-written disclosure *(day/month/year)* | Date of written disclosure referring to non-written disclosure *(day/month/year)* |
|---|---|---|

Claims:

1. A process of removing crystallization inhibitors from a solution comprising one or more reducing monosaccharide sugars and/or corresponding sugar alcohols thereof, c h a r a c t e r i z e d in that said solution is subjected to one or more purification steps selected from nanofiltration and optionally hydrolysis and chromatography, whereby said reducing monosaccharide sugar and/or corresponding sugar alcohol thereof is recovered in the nanofiltration permeate and said crystallization inhibitors are recovered in the nanofiltration retentate.

2. A process as claimed in claim 1, c h a r a c t e r i z e d in that said reducing sugar is xylose.

3. A process as claimed in claim 1, c h a r a c t e r i z e d in that said reducing sugar is fructose.

4. A process as claimed in any one of claims 1 to 3, c h a r a c t e r i z e d in that said crystallization inhibitor is selected from compounds which have a larger molar mass than said reducing sugar or the corresponding sugar alcohol thereof.

5. A process as claimed in claim 4, c h a r a c t e r i z e d in that said crystallization inhibitor is selected from compounds which in their molecule include at least one monosaccharide or corresponding unit more than said reducing sugar or the corresponding sugar alcohol thereof.

6. A process as claimed in claim 4 or 5, c h a r a c t e r i z e d in that said crystallization inhibitor is selected from dimeric and/or oligomeric compounds.

7. A process as claimed in claim 6, c h a r a c t e r i z e d in that said dimeric and/or oligomeric compounds are selected from dimeric and/or oligomeric forms of said reducing sugar and/or the corresponding sugar alcohol thereof.

8. A process as claimed in claim 2, c h a r a c t e r i z e d in that said crystallization inhibitor is selected from xylobiose, xylotriose and xylo-oligosaccharides.

9. A process as claimed in claim 3, c h a r a c t e r i z e d in that said crystallization inhibitor is selected from difructose anhydrides, fructose dianhydrides, diheterolevosanes and diheterolevulosans.

10. A process as claimed in any one of claims 1 to 9, c h a r a c t e r i z e d in that the nanofiltration is carried out at a pressure of 10 to 50 bar, preferably 15 to 40 bar.

11. A process as claimed in any one of claims 1 to 9, c h a r a c - t e r i z e d in that the nanofiltration is carried out at a temperature of 5 to 95 °C, preferably 30 to 60 °C.

12. A process as claimed in any one of claims 1 to 11, c h a r a c - t e r i z e d in that the nanofiltration is carried out with a flux of 5 to 100 liters/$m^2$h.

13. A process as claimed in any one of claims 1 to 9, c h a r a c t e - r i z e d in that the nanofiltration is carried out using a nanofiltration membrane selected from polymeric and inorganic membranes having a cut-off size of 100 to 2500 g/mol.

14. A process as claimed in claim 13, c h a r a c t e r i z e d in that the cut-off size of the nanofiltration membrane is 150 to 1000 g/mol.

15. A process as claimed in claim 14, c h a r a c t e r i z e d in that the cut-off size of the nanofiltration membrane is 150 to 500 g/mol.

16. A process as claimed in any one of claims 13 to 15, c h a r a c - t e r i z e d in that the nanofiltration membrane is selected from ionic membranes.

17. A process as claimed in any one of claims 13 to 16 , c h a r a c - t e r i z e d in that the nanofiltration membrane is selected from hydrophobic and hydrophilic membranes.

18. A process as claimed in any one of claims 13 to 17, c h a r a c - t e r i z e d in that the nanofiltration membrane is selected from cellulose acetate membranes, polyethersulfone membranes, sulfonated polyether sulphone membranes, polyester membranes, polysulfone membranes, aromatic polyamide membranes, polyvinyl alcohol membranes and polypiperazine membranes and combinations thereof.

19. A process as claimed in claim 18, c h a r a c t e r i z e d in that the nanofiltration membrane is selected from sulfonated polyether sulfone membranes and polypiperazine membranes.

20. A process as claimed in claim 18 or 19, c h a r a c t e r i z e d in that the nanofiltration membrane is selected from NF-200, Desal-5 DL, Desal-5 DK, Desal G10 and NTR 7450 membranes.

21. A process as claimed in any one of claims 13 to 20, c h a r a c - t e r i z e d in that the form of the nanofiltration membrane is selected from sheets, tubes, spiral membranes and hollow fibers.

22. A process as claimed in any one of claims 13 to 21, c h a r a c - t e r i z e d in that the nanofiltration membrane is selected from high shear type membranes.

23. A process as claimed in any one of claims 1 to 22, characterized in that the nanofiltration process is repeated at least once.

24. A process as claimed in claim 1, characterized in that said purification steps further comprise hydrolysis.

25. A process as claimed in claim 24, characterized in that said hydrolysis comprises enzymatic hydrolysis.

26. A process as claimed in claim 24, characterized in that said hydrolysis comprises acid hydrolysis.

27. A process as claimed in claim 1, characterized in that said purification steps further comprise chromatographic separation.

28. A process as claimed in claim 27, characterized in that said chromatographic separation is carried out using a column packing material selected from cation exchange resins and anion exchange resins.

29. A process as claimed in claim 28, characterized in that said cation exchange resins are selected from strongly acid cation exchange resins and weakly acid cation exchange resins.

30. A process as claimed in claim 28 or 29, characterized in that said resin is in a monovalent metal form or a divalent metal form.

31. A process as claimed in any one of claims 28 to 30, characterized in that the resin has a styrene skeleton or acrylic skeleton.

32. A process as claimed in any one of claims 1 to 31, characterized in that said solution comprising one or more reducing sugars and/or corresponding sugar alcohols thereof is a biomass hydrolysate.

33. A process as claimed in any one of claims 1 to 32, characterized in that said solution comprising one or more reducing sugars and/or corresponding sugar alcohols thereof is a fraction enriched in said reducing sugar and/or sugar alcohol and obtained from the separation of said reducing sugar and/or sugar alcohol.

34. A process as claimed in claim 33, characterized in that said solution comprising one or more reducing sugars and/or sugar alcohols thereof is obtained from the chromatographic separation of said reducing sugar and/or sugar alcohol.

35. A process as claimed in any one claims 1 to 31, characterized in that said solution comprising one or more reducing sugars and/or corresponding sugar alcohols thereof is a mother liquor obtained from the crystallization of said reducing sugar and/or sugar alcohol.

36. A process as claimed in claim 2, c h a r a c t e r i z e d in that said solution comprising xylose is a spent liquor obtained from a pulping process.

37. A process as claimed in claim 2, c h a r a c t e r i z e d in that said solution comprising xylose is a xylose fraction obtained from the chromatographic separation of xylose from a spent liquor obtained from a pulping process.

38. A process as claimed in claim 2, c h a r a c t e r i z e d in that said solution comprising xylose is a mother liquor obtained from the crystallization of xylose.

39. A process as claimed in claim 3, c h a r a c t e r i z e d in that said solution comprising fructose is a fructose solution obtained from the hydrolysis of starch.

40. A process as claimed in claim 3, c h a r a c t e r i z e d in that said solution comprising fructose is a fructose solution obtained from hydrolyzed and isomerized saccharose.

41. A process as claimed in claim 3, c h a r a c t e r i z e d in that said solution comprising fructose is a fructose fraction obtained from the separation of fructose from a fructose solution obtained from the hydrolysis of starch and/or isomerisation of saccharose.

42. A process as claimed in claim 41, c h a r a c t e r i z e d in that said solution comprising fructose is a fructose fraction obtained from the chromatographic separation of fructose from a solution obtained from the hydrolysis of starch and/or isomerisation of saccharose.

43. A process as claimed in claim 3, c h a r a c t e r i z e d in that said solution comprising fructose is a mother liquor obtained from the crystallization of fructose.

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